

CLAIMS

1. A process for microencapsulating an active principle by coacervation, which consists of

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- the controlled desolvation or coacervation of a polymer dissolved in an organic solvent containing said active principle, said coacervation being induced by addition of a nonsolvent and being reflected by the deposition of the polymer at the surface of the active principle, and then

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- the curing of the polymer deposit by addition of a curing agent, said curing being reflected by the formation of a continuous film coating said active principle,

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characterized in that

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- the solvent for the polymer is a nonchlorinated organic solvent with a boiling point of between 30°C and 240°C and a relative dielectric permittivity of between 4 and 60, advantageously chosen from ethyl acetate, N-methylpyrrolidone, methyl ethyl ketone, acetic acid and propylene carbonate, and mixtures thereof,

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- 45 -

- the nonsolvent is an alcohol or a ketone containing 2 to 5 carbon atoms and preferably 2 or 3 carbon atoms, in particular ethanol ($\epsilon=24$), 2-propanol ($\epsilon=18$), 1,2-propanediol (ϵ between 18 and 24) and glycerol ($\epsilon=40$), or methyl ethyl ketone ($\epsilon=18$),
 - the curing agent is chosen from water, alcohols containing 1 to 4 carbon atoms, on condition that the curing agent is an alcohol that is different than the nonsolvent, and mixtures thereof.
2. The process as claimed in claim 1, characterized in that the nonsolvent and the curing agent are chosen, respectively, from the following pairs: 1,2-propanediol and 2-propanol, glycerol and 1,2-propanediol, glycerol and 2-propanol, 2-propanol and 1,2-propanediol.
3. The process as claimed in claims 1 and 2, characterized in that the polymer is a biodegradable polymer with a weight-average molecular mass (M_w) of between 10,000 and 90,000 g/mol, preferably between 15,000 and 50,000 g/mol, and with a polydispersity index (I_p) of between 1 and 3.5 and preferably between 1.5 and 2.5.

- 46 -

4. The process as claimed in claim 3, characterized in that the polymer is a lactic acid polymer (PLA) or a polymer of lactic acid and of glycolic acid (PLAGA).
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5. The process as claimed in claim 4, characterized in that the polymer is a PLAGA such that Mw is between 15,000 and 25,000, preferably equal to 17,500, Ip is between 1 and 2, and preferably equal to 1.6, and the percentage of glycolic acid is less than 30%, preferably equal to 25%.
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6. The process as claimed in one of claims 1 to 5, characterized in that the polymer concentration in the solvent is between 1 and 10% (w/v) and preferably about 4% (w/v).
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7. The process as claimed in one of the preceding claims, characterized in that the nonsolvent/-solvent ratio by volume is between 1/2 and 1/1.
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8. The process as claimed in one of the preceding claims, characterized in that the coacervation temperature is less than the glass transition temperature of the polymer, preferably less than or less than or equal to 25°C, preferably less than 4°C and more preferably equal to -4°C.
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- 47 -

9. The process as claimed in one of the preceding claims, characterized in that the curing agent also contains a surfactant, the concentration of said surfactant in the curing agent being between 0.1 and 10% (v/v).
10. The process as claimed in one of the preceding claims, characterized in that the surfactant is a sorbitan ester, for example Tween[®] 80 or polyvinyl alcohol.
11. The process as claimed in one of the preceding claims, characterized in that the curing agent/solvent ratio by volume is between 5/1 and 180/1 and preferably between 15/1 and 120/1.
12. The process as claimed in one of the preceding claims, characterized in that the microspheres are cured with stirring at a speed of between 500 and 1500 rpm.
13. The process as claimed in one of the preceding claims, characterized in that the curing temperature is less than or equal to 25°C, preferably less than 4°C and more preferably less than or equal to 0.5°C.
14. The process as claimed in one of the preceding claims, characterized in that when the active

principle forms a dispersion in the polymer solution, the solvent and the nonsolvent have a viscosity that is high enough to stabilize the active principle.

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15. The process as claimed in one of the preceding claims, characterized in that the active principle is dispersed by ultrasound to form a dispersion in the polymer solution, and the coacervation is performed with gentle stirring, preferably of magnetic or mechanical type.

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16. The process as claimed in one of the preceding claims, characterized in that the particle size of the active principle is between 1 and 50 micrometers and preferably between 5 μm and 30 μm .

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17. The process as claimed in one of the preceding claims, characterized in that the solvent is N-methylpyrrolidone, the nonsolvent is ethanol and the curing agent is water.

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18. The process as claimed in one of claims 1 to 16, characterized in that the solvent is ethyl acetate.

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19. The process as claimed in claim 18, characterized in that the solvent is ethyl acetate, the

- 49 -

nonsolvent is 2-propanol and the curing agent is water.

20. The process as claimed in claim 18 or 19,
5 characterized in that the polymer is a 75:25 PLAGA
such that the Mw is between 15,000 and 20,000 and
preferably equal to 17,500, and the Ip is between
1 and 2 and preferably equal to 1.6.
- 10 21. The process as claimed in one of claims 1 to 16,
characterized in that the solvent is acetic acid,
the curing agent is water and the polymer is a
50:50 PLAGA.